

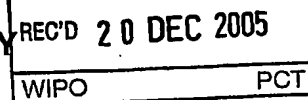
# PATENT COOPERATION TREATY


## PCT

### INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PR/4-33608A/HO 9		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2005/000874		International filing date (day/month/year) 28.01.2005		Priority date (day/month/year) 30.01.2004
International Patent Classification (IPC) or national classification and IPC C07D207/12, A61K31/4015, A61P11/06				
Applicant NOVARTIS AG				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  10.11.2005		Date of completion of this report  16.12.2005		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Zellner, A  Telephone No. +49 89 2399-		



**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2005/000874

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**Box No. I Basis of the report**

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1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-21 as originally filed

**Claims, Numbers**

1-11 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing (*specify*):
  - ☐ any table(s) related to sequence listing (*specify*):

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
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International application No.  
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**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	2-11
	No: Claims	1
Inventive step (IS)	Yes: Claims	
	No: Claims	1-11
Industrial applicability (IA)	Yes: Claims	1-11
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

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**Box No. VI Certain documents cited**

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1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

**see separate sheet**

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

**see separate sheet**

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: US-B1-6 605 623 (KO SOO S ET AL) 12 August 2003 (2003-08-12)  
D2: WO 03/077907 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; LE GRAND, DARREN, MARK; MCCARTHY, C) 25 September 2003 (2003-09-25)  
D3: VARNES, JEFFREY G. ET AL: "Discovery of N-propylurea 3-benzylpiperidines as selective CC chemokine receptor-3 (CCR3) antagonists" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 14(7), 1645-1649 CODEN: BMCLE8; ISSN: 0960-894X, 2004, XP002332418

item V

1. Novelty (Art. 33(2) PCT)

Document D1 discloses compounds which are modulators of CCR3 (abstract). The generic formula disclosed on columns 15-16 overlaps with the generic definition of present claim 1 (D1: formula (I), M is absent, Q is CH<sub>2</sub>, J and K are CH<sub>2</sub>, CHR<sup>5</sup>, CHR<sup>6</sup>, Z is O, R<sup>1</sup> and R<sup>2</sup> are H, R<sup>3</sup> is ... r = 0 (col. 22, l. 34), R<sup>6</sup> is (CH<sub>2</sub>)<sub>r</sub>C(O)R<sup>6b</sup> and R<sup>6b</sup> is phenyl substituted with 0-3 R<sup>6c</sup>). The overlap is considered novelty destroying for present claim 1. The application thus does not meet the requirements of Art. 33(2) PCT. The subject matter of claims 2-11 is considered novel with respect to D1 (X in claim 2 is O).

2. Inventive step (Art. 33(3) PCT)

- 2.1. The presently claimed compounds only differ from the specific examples 152-158 on col. 117 and examples 5-7 on col. 177 of D1 only in that the group T cannot be attached to the N-cyclus via a group CH<sub>2</sub>. According to the general teaching of D1, however, this linker is not required (see col. 16, definition of R<sup>5</sup> and R<sup>6</sup>). The skilled person can thus be expected to provide, starting from the specific examples mentioned, further compounds within the general structure of D1 in order to solve the technical problem of providing alternative CCR3 modulators. The provision of

compounds according to present claims 1-4 is thus not considered based on an inventive step within the meaning of Art. 33(3) PCT.

- 2.2. Document D2 discloses azetidine compounds as CCR3 receptor antagonists (abstract). The presently claimed compounds differ therefrom in the size of the N-ring (see in particular examples 20-57, 66-128, 129, 130, 134-202 of D2). Changing the ring size can be considered obvious for the skilled person who has set himself the task of providing alternative CCR3 receptor modulators because D1 teaches the use of different ring sizes. A combination of the technical teachings of D1 and D2 thus leads to the presently claimed subject-matter, the requirements of Art. 33(3) PCT are thus not met.
- 2.3. The independent claims 5-11 would not appear to relate to subject-matter which can be considered based on an inventive step as long as the product claims the depend on are not in accordance with the requirements of Art. 33(3) PCT.

3. Industrial applicability (Art. 33(4) PCT)

Can be acknowledged for claims 1-11.

**item VI**

Document D3 was published after the priority date of the present application but before its international filing date. Its content would be considered as forming part of the state of the art if the priority of the present application was found to be invalid.

**item VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.